I

addition of claims) are hereby authorized to be charged to our Deposit Account No. 19-0036.

Amendments

In the Claims:

Please substitute the following claim 1 for the pending claim 1:

1. (Once amended) A compound having the Formula I:

 $\begin{array}{c|c} R_7 & R_5 \\ \hline \\ R_8 & R_6 \end{array}$

or a pharmaceutically acceptable salt, prodrug or solvate thereof, wherein

X is one of O, S, NR₉, or CH₂, where R₉ is/hydrogen or C₁-C₁₀ alkyl;

Het is a heteroaryl selected from the group consisting of

 R_1 is selected from the group consisting of hydrogen, optionally substituted alkyl, heteroaryl optionally substituted with one or more groups independently selected from the group consisting of halo, halo(C_{1-6})alkyl, hydroxy(C_{1-6})alkyl, amino(C_{1-6})alkyl, hydroxy, nitro, C_{1-6} alkyl, C_{1-6} alkoxy, aminocarbonyl, carbamoyloxy, C_{1-6} alkylsulfonylamino, C_{1-6} acyl and amino, $C(O)R_{10}$, $CH_2C(O)R_{10}$, $S(O)R_{10}$, and SO_2R_{10} ;

R₂ and R₃ are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, cyano, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkylthio,

alkylsulfinyl, alkylsulfonyl, carboxyalkyl, alkylamino, dialkylamino, aminocarbonyl, alkylaminocarbonyl, aralkylaminocarbonyl, alkylcarbonylamino, aralkylcarbonylamino, alkylcarbonyl, aminosulfonyl, alkylaminosulfonyl, and alkylsulfonyl;

R₅, R₆, R₇, and R₈ are independently selected from the group consisting of hydrogen, halo, haloalkyl, alkyl, alkenyl, alkynyl, hydroxyalkyl, aminoalkyl, carboxyalkyl, alkoxyalkyl, nitro, amino, ureido, cyano, acylamino, amide, hydroxy, thiol, acyloxy, azido, alkoxy, carboxy, carbonylamido and alkylthiol;

R₁₀ is selected from the group consisting of amino, alkyl, alkenyl, alkynyl, OR₁₁, alkylamino, dialkylamino, alkenylamino, dialkylaminoalkenyl, cycloalkyl, heterocycle, heteroaryl, aryl, aralkyl, arylalkenyl, arylalkynyl, and cycloalkylalkylamino;

R₁₁ is selected from the group consisting of hydrogen, optionally substituted alkyl, and an alkalimetal; and

provided that:

- 1) when Het is (ii), and X is O, then R₁₀ is not alkyl, aralkyl, aryl or OR₁₁;
- 2) when Het is (i) or (ii), then X is not NR₉;
- 3) when Het is (iii), then X is not CH2; and
- 4) when Het is (iii), and X is O, then R₁₀ is not OR₁₁.

Please substitute the following claim 10 for the pending claim 10:

10. (Once Amended) A compound of claim 9, wherein:

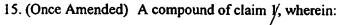
R₅ and R₆ are each hydrogen;

R₃ and R₂ are both H; and

 R_7 and R_8 are selected from the group consisting of hydrogen, halo, halo(C_1 - C_6)alkyl, C_1 - C_6 alkyl, hydroxy(C_1 - C_6)alkyl, amino(C_1 - C_6)alkyl, carboxy(C_1 - C_6)alkyl, alkoxy(C_1 - C_6)alkyl, nitro, amino, C_1 - C_6 acylamino, amide, hydroxy, thiol, C_1 - C_6 acyloxy, C_1 - C_6 alkoxy, carboxy, carbonylamido and C_1 - C_6 alkylthiol.

Please substitute the following claim 15 for the pending claim 15:





Het is (i), (ii), (iii) or (iv);

 R_1 is $C(O)R_{10}$, $CH_2C(O)R_{10}$, or SO_2R_{10} ;

X is O or S;

R₁₀ is amino, optionally substituted C₁-C₆ alkyl, or a heterocycle selected from the group consisting of N-morpholinyl, N-pyrrolidinyl and N-piperazinyl;

R₂, and R₃ are independently hydrogen, C₁-C₆ alkyl, C₁-C₆ alkylthio or C₁-C₆ alkylsulfinyl,

R₅ and R₆ are as defined in claim 1, and

 R_7 and R_8 are independently selected from the group consisting of hydrogen, halo, halo(C_1 - C_6)alkyl, C_{17} C₆ alkyl, hydroxy(C_1 - C_6)alkyl, amino(C_1 - C_6)alkyl, carboxy(C_1 - C_6)alkyl, alkoxy(C_1 - C_6)alkyl, nitro, amino, C_1 - C_6 acylamino, amide, hydroxy, thiol, C_1 - C_6 acyloxy, C_1 - C_6 alkoxy, carboxy, carbonylamido and C_1 - C_6 alkylthiol.

Please substitute the following claim 16 for the pending claim 16:

16. (Once Amended) A compound of Formula I:

or a pharmaceutically acceptable salt, prodrug or solvate thereof, wherein

X is O or S;

Het is a heteroaryl selected from the group consisting of

 R_1 is $C(O)R_{10}$, $CH_2C(O)R_{10}$, or SO_2R_{10} wherein R_{10} is amino, alkyl, N-morpholinyl, N-pyrrolidinyl or N-piperazinyl, all of which are optionally substituted;

3/2

R₂ and R₃ are independently hydrogen, C₁-C₆ alkyl, C₁-C₆ alkylthio or C₁-C₆ alkylsulfinyl;

 R_5 , R_6 , R_7 and R_8 are independently selected from the group consisting of hydrogen, halo, halo(C_1 - C_6)alkyl, C_1 - C_6 alkyl, hydroxy(C_1 - C_6)alkyl, amino(C_1 - C_6)alkyl, carboxy(C_1 - C_6)alkyl, nitro, amino, C_1 - C_6 acylamino, amide, hydroxy, thiol, C_1 - C_6 acyloxy, C_1 - C_6 alkoxy, carboxy, carbonylamido and C_1 - C_6 alkylthiol;

provided that:

- 1) when Het is (ii), and X is O, then R_{10} is not alkyl, aralkyl, aryl or OR_{11} ; and
- 2) when Het is (iii), and X is O, then R₁₀ is not OR₁₁.

Please substitute the following claim 22 for the pending claim 22:

22. (Once Amended) A compound of Formula I:

or a pharmaceutically acceptable salt, prodrug or solvate thereof, wherein

X is O or S;

Het is a heteroaryl selected from the group consisting of

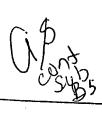
$$-N \longrightarrow R_{2} \qquad -N \longrightarrow R_{2} \qquad -N \longrightarrow R_{3} \qquad -N \longrightarrow R_{1} \qquad -N \longrightarrow R_{1} \qquad -N \longrightarrow R_{2} \qquad -N \longrightarrow R_{3} \qquad (iii) \qquad (iv)$$

 R_1 is $C(O)R_{10}$, wherein R_{10} is amino, N-morpholinyl, N-pyrrolidinyl or N-piperazinyl, all of which are optionally substituted

R₂ and R₃ are independently hydrogen, C₁-C₆ alkyl, C₁-C₆ alkylthio or C₁-C₆ alkylsulfinyl;

 R_5 , R_6 , R_7 and R_8 are independently selected from the group consisting of hydrogen, halo, halo(C_1 - C_6)alkyl, C_1 - C_6 alkyl, hydroxy(C_1 - C_6)alkyl, amino(C_1 - C_6)alkyl,

Why Ships

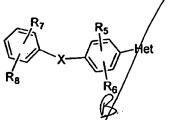


carboxy(C_1 - C_6)alkyl, alkoxy(C_1 - C_6)alkyl, nitro, amino, C_1 - C_6 acylamino, amide, hydroxy, thiol, C_1 - C_6 acyloxy, C_1 - C_6 alkoxy, carboxy, carbonylamido and C_1 - C_6 alkylthiol.

Please insert the following claims 24-27:

24. (New) A compound of claim 15, wherein R₅ and R₆ are both hydrogen.

25. (New) A compound having the Formula I:



or a pharmaceutically acceptable salt, prodrug or solvate thereof, wherein

X is NR₉C(O) or C(O)NR₉, where R₉ is hydrogen or C₁-C₁₀ alkyl; Het is a heteroaryl selected from the group consisting of

R₁ is SO₂R₁₀;

R₂ and R₃ are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, cyano, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkylthio, alkylsulfinyl, alkylsulfonyl, carboxyalkyl, alkylamino, dialkylamino, aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, aralkylaminocarbonyl, alkylcarbonylamino, arylcarbonylamino, aralkylcarbonylamino, alkylcarbonyl, aminosulfonyl, alkylaminosulfonyl, and alkylsulfonyl;

Sub

R₅, R₆, R₇, and R₈ are independently selected from the group consisting of hydrogen, halo, haloalkyl, alkyl, alkenyl, alkynyl, hydroxyalkyl, aminoalkyl, carboxyalkyl, alkoxyalkyl, nitro, amino, ureido, cyano, acylamino, amide, hydroxy, thiol, acyloxy, azido, alkoxy, carboxy, carbonylamido and alkylthiol;

R₁₀ is selected from the group consisting of amino, alkyl, alkenyl, alkynyl, OR₁₁, alkylamino, dialkylamino, alkenylamino, dialkylaminoalkenyl, cycloalkyl, heterocycle, heteroaryl, aryl, aralkyl, arylalkenyl, arylalkynyl, and cycloalkylalkylamino; and

R₁₁ is selected from the group consisting of hydrogen, optionally substituted alkyl, and an alkalimetal.

26. (New) A compound having the Formula I:

$$R_8$$
 R_6
 R_6
 R_6

or a pharmaceutically acceptable salt, prodrug or solvate thereof, wherein

X is one of O, S, NR₉, CH₂, NR₉C(O), or C(O)NR₉, where R₉ is hydrogen or C_1 - C_{10} alkyl;

Het is a heteroaryl selected from the group consisting of

$$-N \longrightarrow R_{2} \qquad -N \longrightarrow R_{2} \qquad -N \longrightarrow N \longrightarrow R_{1} \qquad -N \longrightarrow N \longrightarrow N$$

$$R_{3} \qquad (ii) \qquad (iii) \qquad R_{3} \qquad (iiii) \qquad (iv)$$

 R_1 is selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted heteroaryl, $C(O)R_{10}$, $CH_2C(O)R_{10}$, $S(O)R_{10}$, and SO_2R_{10} ;

R₂ and R₃ are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, aryl, cyano, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkylthio, alkylsulfinyl, alkylsulfonyl, carboxyalkyl, alkylamino, dialkylamino, aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, aralkylaminocarbonyl, alkylcarbonylamino, arylcarbonylamino, aralkylcarbonylamino, alkylcarbonyl, aminosulfonyl,

alkylaminosulfonyl, and alkylsulfonyl;

R₅, R₆, R₇, and R₈ are independently selected from the group consisting of hydrogen, halo, haloalkyl, alkyl, alkenyl, alkynyl, hydroxyalkyl, aminoalkyl, carboxyalkyl, alkoxyalkyl, nitro, amino, ureido, cyano, acylamino, amide, hydroxy, thiol, acyloxy, azido, alkoxy, carboxy, carbonylamido and alkylthiol;

R₁₀ is selected from the group consisting of amino, alkyl, alkenyl, alkynyl, OR₁₁, alkylamino, dialkylamino, alkenylamino, dialkylaminoalkenyl, cycloalkyl, heterocycle, heteroaryl, aryl, aralkyl, arylalkenyl, arylalkynyl, and cycloalkylalkylamino;

R₁₁ is selected from the group consisting of hydrogen, optionally substituted alkyl, and an alkalimetal; and

wherein said compound is ³H or ¹⁴C radiolabeled.

27. (New) The method according to claim 19, wherein the method is for treating, preventing or ameliorating neuronal loss following global or focal ischemia, treating or ameliorating neurodegenerative conditions, treating, preventing or ameliorating pain or tinnitus, treating, preventing or ameliorating manic depression, providing local anesthesia, treating arrhytmias, or treating convulsions.

Coux